Intra-articular Hyaluronan Injections for Osteoarthritis

Description

Intra-articular injection of hyaluronan (HA) into osteoarthritic joints is thought to replace HA, restore the viscoelastic properties of the synovial fluid, and improve pain and function. The majority of studies to date have assessed HA injections for knee osteoarthritis, and this is the U.S. Food and Drug Administration (FDA) -approved indication. Other joints, such as the hip and shoulder, are currently being investigated for intra-articular HA treatment of osteoarthritis (OA).

Hyaluronan (HA) is a naturally occurring macromolecule that is a major component of synovial fluid and is thought to contribute to its viscoelastic properties. Chemical crosslinking of hyaluronan increases its molecular weight; crosslinked hyaluronans are referred to as hylans. In osteoarthritis (OA), the overall length of HA chains present in cartilage and the HA concentration in the synovial fluid are decreased. Intra-articular injection of HA (IAHA) has been proposed as a means of restoring the normal viscoelasticity of the synovial fluid in patients with OA. This treatment has been called viscosupplementation. Currently, no curative therapy is available for OA, and thus the overall goals of management are to reduce pain and prevent disability.

Regulatory Status

Six preparations of intra-articular (IA) hyaluronan have been approved by the FDA as an alternative to nonsteroidal anti-inflammatory drug therapy in the treatment of OA of the knee (Synvisc® and Synvisc-One®, Genzyme; Hylgan®, Fidia; Supartz®, Smith and Nephew; OrthoVisc®, Anika; and Euflexxa®, previously named Nuflexxa, Savient). All products are manufactured from rooster combs except for Euflexxa and Orthovisc, which are produced from bacterial fermentation. Also, Synvisc undergoes additional chemical crosslinking to create hylans with increased molecular weight (6,000 kDa) compared to Hyalgan (500-730 kDa) and Supartz (620-1170 kDa). The differing molecular weights of the products lead to different half-lives; the half-life of Hylgan or Supartz is estimated at 24 hours, while the half-life of Synvisc may range up to several days.
Intra-articular hyaluronic acid is “indicated for the treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy, and to simple analgesics, e.g., acetaminophen.” The product inserts further indicate that Synvisc® and Euflexxa® should be injected intra-articularly into the knee joint once per week for a total of 3 injections over a 2- to 3-week period. In contrast, 5 weekly injections are recommended for the Hyalgan® and Supartz® products, and 3–4 weekly injections are recommended for OrthoVisc®. In February 2009, the FDA approved the use of single-dose hylan G-F 20 (Synvisc-One™) for the treatment of OA of the knee. The In 2011, the FDA approved the use of the single-dose cross-linked hyaluronate Gel-One® (also known as Gel-200) for the treatment of OA of the knee.

In 2000, the FDA approved removal of a precautionary statement from the package inserts for Hyalgan and Synvisc that stated that the safety and efficacy of repeat courses have not been established.

The FDA has not approved intra-articular hyaluronan for joints other than the knee.

Policy

Intra-articular hyaluronan injections may be considered medically necessary for treatment of painful osteoarthritis of the knee in patients who have insufficient pain relief from conservative nonpharmacologic therapy and simple analgesics.

Repeated courses of intra-articular hyaluronan injections of the knee may be considered medically necessary under the following conditions:

- Significant pain relief achieved with the prior course of injections; and
- At least 6 months have passed since completion of the prior course.

The use of intra-articular hyaluronan in the knee when the above criteria are not met, and in joints other than the knee, is considered investigational.

Policy Guidelines

Appropriate candidates for hyaluronan injections are those who have failed conservative therapy with nonsteroidal anti-inflammatory drugs (NSAIDs) or who have contraindications to NSAID therapy. Plans may also require candidates for hyaluronan injections to have failed intra-articular injections of corticosteroids.

A course of hyaluronan injections is defined according to labeled indications for each product; one formulation involves a single injection, others use multiple injections. For example, Synvisc-One® is a single 6-mL injection treatment regimen. For a single course of treatment, the single injection formulation should not be followed with subsequent doses of the multiple-injection formulations.

When determining the timing of repeated courses, the prior course is assumed to have been completed at the date of the last injection of the series of injections.

The procedure may be billed using a combination of CPT codes to describe the procedure and J codes to describe the hyaluronic acid product.
CPT code

20610: Arthrocentesis, aspiration or injection; major joint or bursa

The initial office visit to initiate hyaluronan therapy may be billed using an evaluation and management CPT code; however, the use of both CPT code 20610 and an evaluation and management CPT code during subsequent visits for the sole purpose of hyaluronan injections is not routinely warranted.

The following HCPCS codes are specific to the various hyaluronan products:

J7321: Hyaluronan or derivative, Hyalgan or Supartz, for intra-articular injection, per dose
J7323: Hyaluronan or derivative, Euflexxa, for intra-articular injection, per dose
J7324: Hyaluronan or derivative, Orthovisc, for intra-articular injection, per dose
J7325: Hyaluronan or derivative, Synvisc or Synvisc-One, for intra-articular injection, 1 mg
J7326: Hyaluronan or derivative, Gel-One, for intra-articular injection, per dose

This policy was created in 1998 and updated regularly with searches of the MEDLINE database. The most recent literature search was performed through January 23, 2013. Following is a summary of key literature to date.

Knee

Systematic Reviews

This policy was originally based on a 1998 TEC Assessment on intra-articular hyaluronan (IAHA) for osteoarthritis (OA) of the knee, (1) and in 2004, TEC published a Special Report on IAHA for OA of the knee. (2) Overall, the 2004 review found that the evidence was still consistent with that presented in the 1998 TEC Assessment, showing a statistically significant effect in almost all studies, although the magnitude and clinical significance of the effect may be small. There were inadequate data to determine the clinical efficacy of hyaluronan injections in joints other than the knee.

A 2005 Cochrane review of viscosupplementation for OA of the knee evaluated a total of 63 clinical trials. (3) The conclusions of the Cochrane review are consistent with the 2004 TEC Special Report. While hyaluronan has some beneficial effect, the magnitude and clinical significance of the effect may be small. An April 2006 update of the Cochrane review evaluated a total of 76 clinical trials. (4) The Cochrane review came to the same conclusions it had made previously, that HA treatment was more effective than placebo, most notably in the 5 to 13 weeks after treatment.

In 2007, the TEC Evidence-based Practice Center published a technology assessment for the Agency for Healthcare Research and Quality (AHRQ) on the treatment of primary and secondary OA of the knee. (5) The report concluded that results from 42 trials (n=5,843) generally show positive effects of viscosupplementation on pain and function scores compared to placebo for patients with primary OA of the knee. However, the evidence on viscosupplementation was accompanied by considerable uncertainty due to variable trial quality,
potential publication bias, and unclear clinical significance of the changes reported. Trials of hylan G-F 20 (Synvisc, 6,000 kDa), the highest molecular weight cross-linked product, generally reported better results than other trials.

Rutjes et al. published a 2012 meta-analysis of 89 trials (12,667 patients) on viscosupplementation for OA of the knee. (6) The main results showed that viscosupplementation moderately reduced pain (effect size: -0.37). However, several limitations of this body of literature were noted. Trial quality was low, there was considerable between-trial heterogeneity, and an asymmetrical funnel plot suggested publication bias. Five unpublished trials showed an insignificant effect size of -0.03, while analysis of 18 large trials with blinded outcome assessment showed an effect size of -0.11, which is of uncertain clinical significance. Viscosupplementation was also associated with an increased risk for serious adverse events.

Comparative Effectiveness. A 2007 meta-analysis of 13 trials found no superior effectiveness of high-molecular weight hylan (Synvisc) over medium-molecular weight HA (Orthovisc), or low-molecular weight HA (Ostenil, unavailable in the U.S.). (7) A 2012 meta-analysis of 74 trials found that due to the heterogeneity of the studies and outcomes, it was not possible to conclude that one brand is more efficacious than another. (8)

In 2009, Bannuru et al. conducted a meta-analysis of 7 randomized controlled trials (RCTs) (610 patients) that compared pain relief achieved with IAHA or intra-articular (IA) corticosteroids in OA of the knee. (9) Trial quality was fair, heterogeneity was moderate, and there was evidence of publication bias. At week 2, the effect size favored corticosteroids; at week 4, the effect size suggested equal efficacy; and at weeks 12 and 26, effect sizes favoring IAHA were found.

Durability. Bannuru et al. published another meta-analysis of IAHA for knee OA in 2011 that evaluated 54 randomized clinical trials, 49 of which compared the effects over time of IAHA to placebo for pain relief. (10) Trial quality and conduct varied. By week 4, the effect size favored IAHA, peaked at 8 weeks, and decreased by week 24 to a lesser residual effect.

Repeat Courses. In a 2005 meta-analysis, Pagnano and Westrich concluded that repeat courses of HA for OA of the knee were as safe and effective as a single course of HA injections. (11)

Randomized Controlled Trials

As indicated by the systematic reviews described above, there are a large number of randomized controlled trials that have evaluated the efficacy of IAHA for OA of the knee. Following is a description of some of the key studies and more recent randomized controlled trials.

Durability. A multicenter, placebo-controlled, double-blind RCT from 2010 administered 5 weekly Hyalgan or saline placebo IA injections to 335 patients with OA of the knee (335 knees) and assessed survival of response at 3, 6, 9, and 12 months. (12) Survival of response was defined using the Lequesne algofunctional index (LFI), an international index for scoring pain and function in OA using a 0-24 point scale. The LFI is a modification of the Western Ontario and McMaster University (WOMAC) Index of Osteoarthritis, a 24-item self-administered questionnaire that assesses pain, stiffness, and function in OA patients. The LFI is not as well-validated as the WOMAC. In this study, a 1-point decrease in LFI score defined the onset of improvement, and a 1-point increase in LFI score defined recurrence. These changes may not be clinically relevant. There was no statistically significant difference between groups in the time...
to recurrence (Hyalgan group, 172 days; placebo group, 204 days, p=0.26). The total number of adverse events in the Hyalgan and placebo groups was 133 and 178, respectively. Local injection site pain, joint pain exacerbation, and “infections in general” were reported more often in the placebo group.

Repeat IAHA. Results from an RCT on the effects of repeat IAHA for knee OA (the AMELIA project) were published in 2011. (13) In this trial of 306 patients, 5 injections of IAHA or placebo were given weekly for 4 treatment cycles. Patients were followed a total of 40 months, including a 6-month follow-up after the first and second cycles and a 1-year follow-up after the third and fourth cycles. Patients were not permitted to use non-steroidal anti-inflammatory medications 1 week before follow-up evaluations, nor were they permitted to receive corticosteroid injections in the treatment knee during the entire study period. After each treatment cycle, more patients in the IAHA group progressively responded (from 71.1% to 80.5%) compared to the placebo group (from 67.8% to 65.8%) according to Osteoarthritis Research Society International (OARSI) 2004 criteria. At the end of follow-up, 120 patients responded to IAHA or 22% more than the 100 patients that responded to placebo (relative risk [RR], 1.22, 95% CI: 1.07 to 1.41; p=0.004). Adverse events included local bleeding, mild pain, or allergic reaction and occurred at a rate of 0.029 per cycle in both groups. Serious adverse events did not occur. The authors noted repeated injections of IAHA progressively increased the number of patients responding and demonstrated a positive carry-over effect for up to 1 year, but whether this suggests remission or alteration of the course of OA could not be determined.

Single dose viscosupplementation. In 2009, the FDA approved the use of single-dose hylan G-F 20 (Synvisc-One™) for the treatment of knee OA. This approval was based on a double-blind, randomized clinical trial that compared a single 6-mL IA injection of either hylan G-F 20 or saline in 253 osteoarthritic knees. (14) At 26 weeks, there was a significant reduction in pain (>20%) in both groups, as measured by the Western Ontario and McMaster University (WOMAC) A (pain) subscale. The improvement at 26 weeks in the treatment group was greater than in the control group (-0.84 vs. -0.69, respectively, p=0.047), and the magnitude of the improvement is similar to that noted in trials with 3 to 5 injections of hylan G-F 20 versus placebo when the scores are adjusted for the overall scale. The difference between groups, while statistically significant at 26 weeks, had not shown statistical significance at 12 weeks. Thus, this formulation appears to provide improvements similar to those noted for existing agents.

In 2011, the FDA approved the use of a single dose of Gel-One®, also known as Gel-200, a cross-linked formulation of hyaluronic acid. Approval was based on a multicenter randomized double-blind placebo controlled trial in 377 patients. (15) The percentage of patients reporting a 30% or greater improvement in the WOMAC pain subscore was 56.8% at week 3 compared to 47.2% for placebo. The percentage of patients reporting a 50% or greater improvement in the WOMAC pain subscore was 42.8% at week 3 compared to 28.0% for placebo. Significant differences between the groups in mean scores persisted throughout the 13-week follow-up period.

Comparative Effectiveness. An RCT (16) compared 3 injections of either high-molecular weight HA (Synvisc) vs. medium-molecular weight HA (Orthovisc), or low-molecular weight HA (Ostenil, unavailable in the U.S.) in 660 patients with OA of the knee. At 6 months, there was no difference between groups in any outcome measure. In 2 randomized controlled, non-inferiority trials, published in 2011, different hyaluronans were also compared and found to have similar outcomes. In one trial of 381 patients, highly purified hyaluronic acid (Sinovial®) was found to be equivalent to 0.8% hylan G-F20 (Synvisc®). (17) In the other trial of 276 patients, a medium
molecular weight hyaluronan product (F60027, Structovial) was also found to be equivalent to hylan G-F 20 (Synvisc®). (18)

Conclusions. There are a large number of RCTs completed on treatment of OA of the knee with HA, and numerous systematic reviews of these trials. The majority of systematic reviews conclude that there is a modest beneficial effect of treatment, and the clinical significance of the magnitude of difference is uncertain. The strength of these conclusions is reduced by limitations in the literature, which include variable quality of studies, a large degree of heterogeneity in outcomes, and possible publication bias. In studies that compared IAHA with IA steroids, IAHA had a slower onset of action and longer duration. Several studies have compared different types of HA, with no clear differences in efficacy found between different types.

**Joints Except the Knee**

Colen et al. conducted a 2012 systematic review of prospective trials of IAHA for joints other than the knee. (19) In addition to non-randomized prospective studies, the search identified 5 RCTs for the hip, 1 for the shoulder, 4 for the ankle, 5 for the carpometacarpal-1 joint, 1 for the lumbar facet joint, and 1 for the first metatarsophalangeal joint. Examination of the literature for each joint found evidence for a positive effect of IAHA when compared to baseline, with limited evidence that IAHA is superior to placebo, and no evidence that IAHA is better than corticosteroids or other conservative therapies. Following is a summary of systematic reviews and primary evidence by joint.

**Ankle**

Migliore and colleagues conducted a review of 7 studies on IAHA for ankle OA, identified from the period of 2006-2009, that included 3 small RCTs with a total of 75 patients, and 4 case series. (20) For 2 of the RCTs, IAHA was compared to saline injection, and the results showed benefit on some outcome measures but not others. The third RCT compared IAHA to exercise therapy and reported no differences in outcomes. The authors were unable to do a meta-analysis due to the limited number of studies and study heterogeneity.

In 2012, DeGroot et al. reported on an RCT of 64 patients with ankle OA that compared a single IAHA to a single IA saline injection. (21) At 6 weeks and 12 weeks, there were no significant differences in improvement between treatment groups on the American Orthopaedic Foot & Ankle Society clinical rating score, the Ankle Osteoarthritis Scale score, and the patient-reported visual analog pain scale (VAS).

**Foot**

There is a very limited amount of evidence on IAHA injections in the foot. Munteanu and colleagues reported on an RCT of a single IAHA injection in 151 patients with first metatarsophalangeal joint OA. (22) At 1, 3, and 6 months’ follow-up, there were no significant differences between the IAHA and placebo groups on the Foot Health Status Questionnaire.

**Hand**

Two small RCTs that enrolled a total of 100 patients evaluated HA injections compared to steroid injections for arthritis of the thumb. (23, 24) Fuchs et al. (24) reported that steroid injections were superior at 2-3 weeks post-treatment but that IAHA was superior at 6 months’ follow-up. Stahl et al. (23) reported essentially equivalent outcomes between steroid injections.
and IAHA, although IAHA was superior to steroids for some aspects of fine motor function. The results of these trials are not sufficient to determine the efficacy of IAHA for thumb arthritis and are not sufficient for determining comparative efficacy to steroids.

**Hip**

A 2008 systematic review of 2 RCTs and 9 cohort studies concluded that viscosupplementation therapy with HA appears to be “a safe and effective method in the treatment of hip OA resistant to conventional treatment modalities.” (25) In their 2012 systematic review, Colen et al. identified 3 RCTs that compared IAHA with placebo, 1 that compared IAHA with IA anesthetic, and 1 that compared hyaluronans of different molecular weights. (19) These 3 trials showed a statistical effect favoring IAHA treatment. However, the effect size was small compared to saline injections, and there were not significant differences between IAHA and other conservative treatments such as steroid injections.

The largest RCT randomized 101 patients to receive either HA injections or saline. (26) There was a small reduction in pain with walking in patients treated with HA injections over the 3-month evaluation period. An industry-sponsored RCT compared a single 2.5 mL IAHA (Adant, 900 kDa, unavailable in the U.S.) to saline injection for treatment of hip OA in 85 patients. (27) At 3 months, there were no significant differences between groups in any outcome measure. The number of patients who experienced mild to moderate treatment-related adverse events (injection-site pain, pain flare, hematoma, pruritus) did not differ between groups. Atchia and colleagues reported on a randomized, controlled trial (RCT) of 77 patients with hip OA who were potential candidates for total hip replacement. (28) In this study, patients were randomized to receive standard care or an injection of saline, hyaluronan or methylprednisolone and followed for 8 weeks. Significant improvement was only seen in the steroid group in the numerical rating scale for worst pain, and the Western Ontario and McMaster Osteoarthritis Index for pain and function. No improvements were reported in the IAHA group.

In an industry-sponsored, single-center, randomized, double-blind, active-controlled trial, published in 2009, 42 patients with OA of the hip were randomly assigned to receive 2 monthly injections of high-molecular weight IAHA (Hyalubrix® - unavailable in the U.S.) or IA mepivicaine, a local anesthetic. (29) At 3 and 6 months, there was a significant decrease in the LFI in the IAHA group compared to the mepivicaine group (5.15 vs. 6.53 at 3 months; 3.94 vs. 6.41 at 6 months, both respectively). The only reported adverse event was injection-site pain occurring in 1 patient in each group.

**Shoulder**

A 2010 meta-analysis of 19 blinded RCTs examined the use of viscosupplementation for chronic painful shoulder in a total of 2,120 patients. (30) A variety of shoulder disorders were included, e.g., adhesive capsulitis, rotator cuff tear, shoulder impingement syndrome, and frozen shoulder. Sample size ranged from 20 to 660 patients, mean trial duration was 3.5 weeks, and mean Jadad score was 3.5 ± 1.5. Ten trials (1,435 patients) reported pain outcomes. The combined effect size (standardized mean difference) for categorical and continuous pain ratings favored IAHA (0.39). There was no heterogeneity and no evidence of publication bias. Because the studies included in the meta-analysis were of short duration and included a variety of shoulder diseases, they do not provide conclusive evidence of the effectiveness of IAHA in OA of the shoulder.
The largest trial is an industry-sponsored RCT of 660 patients with persistent shoulder pain due to glenohumeral joint OA, rotator cuff tear, and/or adhesive capsulitis compared 3 weekly injections versus 5 weekly injections of sodium hyaluronate (Hyalgan) versus 5 weekly injections of saline. (31) Approximately 60% of patients had OA, although the majority of those with OA also had rotator cuff disorders or capsulitis. Sixty-nine percent (n=456) of the patients had a follow-up visit at 26 weeks. There was no significant difference among groups in the primary outcome measure, shoulder pain with movement at 13 weeks. Analysis of predefined, stratified subgroups revealed no significant differences in reported pain at 13 weeks but a statistically significant decrease of 7.5 and 7.8 mm (on a 100-mm VAS scale) in reported pain in both treatment groups at 26 weeks compared to placebo among patients with OA. In those without OA, there was no significant improvement with either regimen. Of note, this appears to be an as-treated analysis of the OA subgroup data, and the difference may not be clinically important.

In 2013, Kwon et al. reported a multicenter randomized double-blind placebo-controlled trial of IAHA in 300 patients with glenohumeral OA. (32) Intent-to-treat analysis found similar improvement in VAS for pain (19.88 mm for IAHA and 16.29 mm for placebo) and in the Outcome Measures in Rheumatoid Clinical Trials-Osteoarthritis Research Society International (OMERACT-OARSI) high responder rate (40.8% for IAHA and 34.9% for sham). In a subset of patients there was a statistically significant difference in VAS of 4.0 mm on a 100-mm scale and 8.37% on the OMERACT-OARSI. However, the clinical significance of these differences is uncertain.

Other

Data from small pilot studies, and case series have been reported using hyaluronan for arthritis of the spine and for lateral condylitis of the elbow (tennis elbow).

Conclusions. The evidence on the efficacy of IAHA for joints other than the knee is less robust. While some studies show benefit, others do not, and systematic reviews have not concluded that there is a clinically significant benefit. This evidence is not sufficient to conclude that IAHA treatment of joints other than the knee improves outcomes.

Ongoing Clinical Trials

A search of online site ClinicalTrials.gov in January 2013 identified a number of open trials with IAHA. These include Phase III and Phase IV trials evaluating IAHA for OA of the knee (NCT01372475, NCT01543737, NCT01557868, and NCT01335321), and a pivotal multicenter trial of Hylan G-F 20 for OA of the hip (NCT01618708).

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 3 physician specialty societies and 5 academic medical centers (6 reviewers) while this policy was under review in 2011. Most reviewers agreed with the conclusions of this policy. In addition, those providing input supported the
interval between and criterion for repeat injections. In response to a question about total number of treatment courses, there was no consensus; several noted that continued patient improvement with repeat treatment is an important finding.

Summary

Intra-articular injection of hyaluronan (IAHA) into osteoarthritic joints is thought to replace hyaluronan, restore the viscoelastic properties of the synovial fluid, and improve pain and function. The largest amount of evidence is on treatment of osteoarthritis (OA) of the knee. Individual trials show inconsistent results in pain and functional outcomes for IAHA compared to placebo or active control. Meta-analyses of RCTs, however, support the clinical effectiveness of IAHA in OA of the knee. In general, studies report that IAHA had later onset but longer duration of action compared to intra-articular corticosteroid injections. A recent RCT found repeated injections of IAHA progressively increased the number of patients responding to IAHA. A positive carry-over effect for up to 1 year was also noted after repeated injections of IAHA. Therefore, based on a compilation of available evidence, IAHA injections for osteoarthritis of the knee appear to reduce pain and improve health outcomes and may be considered medically necessary.

IAHA continues to be investigated for off-label uses in other joints. Current evidence on these off-label uses is limited, consisting of small RCTs and case series. Some RCTs on IAHA injections for OA of the ankle, foot, hand and shoulder have shown treatment benefits; however, these studies are not consistent in reporting improvements that are significantly greater than placebo and/or control treatments. RCTs on IAHA injections for OA of the hip have also been inconsistent, with some RCTs reporting improvements in outcomes with IAHA hip injections and others reporting no improvement. Currently, given the limited and inconsistent available data, these uses are considered investigational.

Practice Guidelines and Position Statements

In 1995, the American College of Rheumatology (ACR) published guidelines for the treatment of osteoarthritis (OA) of the knee, which recommended acetaminophen as first-line therapy, followed by low-dose ibuprofen, and then full-dose nonsteroidal anti-inflammatory drugs (NSAIDs), when necessary. In 2000, the ACR published updated guidelines on the management of hip and knee OA. These guidelines recommend nonpharmacologic approaches and drug therapy for management of hip and knee OA. Intra-articular hyaluronan (IAHA) or glucocorticoids are considered alternative approaches to oral agents for knee OA, based on studies demonstrating effectiveness in reducing knee pain. However, the guidelines noted the absence of studies demonstrating the efficacy of IAHA or glucocorticoids for hip OA. Updated guidelines from 2012 addressed OA of the hand, hip, and knee. (34) A conditional recommendation was given for IAHA to treat OA of the knee. The ACR recommends not using IAHA for OA of the hand. For OA of the hip, the ACR explicitly makes no recommendation regarding treatment with IAHA.

The Osteoarthritis Research Society International (OARSI) guidelines, (35) developed by consensus after review of existing guidelines and systematic reviews, recommend:

Injections of IA [intra-articular] hyaluronate may be useful in patients with knee or hip OA [osteoarthritis]. They are characterised by delayed onset, but prolonged duration, of symptomatic benefit when compared to IA injections of corticosteroids.
The recommendation is made with a strength of 64% (CI: 43–85%).

The 2009 Bannuru et al. meta-analysis, (9) noted above, was cited in a 2010 evidence update by OARSI. (36) In an accompanying editorial, OARSI authors note that IAHA “has a time-dependent trajectory of therapeutic effect. Thus, the time point at which its outcome is assessed will influence its apparent effectiveness.” (37)

The American Academy of Orthopaedic Surgeons’ (AAOS) 2008 guideline on the non-arthroplasty treatment of OA of the knee indicates a recommendation cannot be made for IAHA for mild to moderate symptomatic knee OA. (31) The guideline notes available evidence is inconclusive. However, this AAOS guideline does indicate intra-articular corticosteroid injections are suggested for short-term pain relief for symptomatic knee OA, based on fair evidence.

The 2009 AAOS Clinical Practice Guideline on glenohumeral joint osteoarthritis (38) includes a weak grade C recommendation that “the use of injectable viscosupplementation is an option when treating patients with glenohumeral [shoulder] osteoarthritis.” Grade C recommendations are based on poor-quality evidence. In this instance, the recommendation is based on a single case series of 30 patients with OA of the glenohumeral joint who received 3 weekly IA injections of Synvisc. (39) At 1, 3, and 6 months, clinically significant improvements were seen in pain, function, and quality-of-life measures.

Guidelines published by the National Institute for Health and Clinical Excellence (NICE) do not recommend IAHA injections for the treatment of OA because “the cost-effectiveness estimate is outside the realms of affordability” to the National Health Service. (7) However, guideline developers state “Overall, the evidence suggests that hyaluronans and hylan derivatives seem to be superior to placebo in terms of efficacy and quality of life outcomes in patients with OA in the knee at different post-injection periods but especially at the 5- to 13-week post-injection period.” Toxicity of IAHA was noted to be small.

References:


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